Lentigo Maligna With Spread Onto Oral Mucosa

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Background: Lentigo maligna (LM) is a form of melanoma in situ most often seen in white patients on sun-exposed areas, primarily the head and neck. Spread of LM onto the conjunctiva has been reported. There have been no reports of LM extending onto oral mucosa.

Observations: We report 4 cases of LM in white women with contiguous spread from perioral areas to oral mucosa. The locations of the primary lesions were the vermilion of the lip, vermilion and perioral skin, cheek, and cutaneous aspect of the lip. Three cases showed focal histopathologic evidence of invasion during the course of the disease. The lesions ran a prolonged course characterized by repeated recurrences after surgery. Three of the cases required a complicated reconstruction after surgical excision. Mohs surgery with rush permanent (paraffin-embedded) sections resulted in a long remission in 2 cases, while in 1 patient, treatment with carbon dioxide laser was unsuccessful.

Conclusions: In a perioral distribution, LM can spread onto oral mucosa. This clinical presentation may cause significant long-term morbidity, as indicated by a high recurrence rate and/or progression to invasive melanoma. The oral mucosa should be examined in patients with atypical pigmented perioral lesions.

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Lentigo Maligna (LM) is a type of melanoma in situ with unique clinical and histopathologic features.1 It occurs almost exclusively in whites and shows a slight female preponderance.2 Lentigo maligna usually presents as a poorly circumscribed, variably colored patch on sun-exposed areas, primarily the head and neck. The cheek is the most common site. The margins of LM are often difficult to evaluate as a result of mottled pigmentation and a background of solar lentigines and chronic photodamage.2 Long-term cumulative UV radiation is the most widely recognized risk factor for the development of LM.3,4 Lentigo maligna melanoma (LMM), the invasive form of LM, is the most common subtype of malignant melanoma on the face.3 Lentigo maligna occurs less commonly on the trunk and extremities. Lesions previously reported on the subungual area,6,7 fingers,8,9 toes,10 hand,11 foot,11 scrotum,12 penis,13 and oral mucosa14,15 would be classified today as acral lentigious melanoma or another histologic type.16,17 The conjunctiva may be involved when LM on the eyelids and/or periorbital areas spreads onto conjunctival mucosa.18-20 A case of melanoma in situ involving the oral mucosa, lips, and perioral skin was reported and was believed to have spread from the oral mucosa to the perioral skin.21 One of us (L.M.C.) recently reported extension of recurrent LM of the cheek onto buccal mucosa (case 3 in this series).22

Herein, we report 4 cases of LM with contiguous spread from perioral skin and/or vermilion of the lip onto oral mucosa. To our knowledge, this clinical presentation has not been previously reported. All patients experienced significant morbidity. We review the complicated course and prognosis of these patients and discuss treatment options and the challenge of permanent cure. The clinical data and response to treatment in the cases studied are summarized in the Table.

REPORT OF CASES

CASE 1

Biopsy specimens of the primary and recurrent lesions (the latter shown in Figure 1 and Figure 2) demonstrated LM. The recurrent lesions were treated with carbon dioxide laser excision fol-
allowed by peripheral vaporization. The buccal mucosal specimen removed during the laser excision revealed extensive LMM in vertical growth phase with an invasive desmoplastic component and positive margins. Three months later, biopsy specimens from residual pigmented oral lesions taken by repeat laser excision showed residual LM in the oral commissure.

CASE 2

Biopsy specimens of the primary lesion (Figure 3) revealed LM. The lesion was excised with a 5-mm margin using rush permanent sections. The upper lip was repaired with a rhombic flap and the lower lip, with an advancement flap. Two years later, 3 tan to brown pigmented patches were noted on the right buccal mucosa and lower labial mucosa (Figure 4). Biopsy specimens confirmed recurrent LM. Negative margins were obtained after 3 stages of excision with rush permanent sections, and the defect was repaired with a full-thickness skin graft from the groin. No recurrences or new atypical lesions have been noted 5 years after excision.

CASE 3

A biopsy specimen of the primary lesion on the left cheek showed LM. The lesion recurred several times and was excised after each recurrence; advancement flap was used once for the repair. Ten years after the appearance of the primary lesion, a recurrent lesion was noted on the left cheek and oral commissure. This was treated with wide excision and reconstruction with a cervicofacial rotation flap. Pathologic analysis showed a 3-mm-thick LMM, but the margins were ambiguous. Three years later, extensive pigmentation was noted along the scar from the

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**Clinical Data and Response to Treatment in the Cases Studied**

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Initial Lesion</th>
<th>Treatment</th>
<th>Recurrent Lesions</th>
<th>Progression to LMM</th>
<th>Patient Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/70</td>
<td>Lower lip 20 y ago</td>
<td>Excision, negative margins</td>
<td>Upper and lower lips and buccal mucosa</td>
<td>Yes</td>
<td>Carbon dioxide laser, positive margins</td>
</tr>
<tr>
<td>2/F/57</td>
<td>Long-standing lesion on right oral commissure, lips, and adjacent skin</td>
<td>Narrow excision with RPS, negative margins</td>
<td>Buccal and labial mucosa</td>
<td>No</td>
<td>Excision with RPS, no recurrences in 5 y</td>
</tr>
<tr>
<td>3/F/51</td>
<td>Left cheek 20 y ago</td>
<td>Excision, negative margins</td>
<td>Recurrences on flap scars, oral commissure, upper lip, buccal mucosa</td>
<td>Yes</td>
<td>Excision with RPS, no recurrences in 6 y</td>
</tr>
<tr>
<td>4/F/81</td>
<td>Left upper lip 12 y ago; to commissure, vermilion, labial mucosa 1 y later</td>
<td>Narrow excision, negative margins</td>
<td>Recurrences on upper lip, cheek, melolabial fold</td>
<td>Yes</td>
<td>Excision, positive margins</td>
</tr>
</tbody>
</table>

*RPS indicates rush permanent section; LMM, lentigo maligna melanoma.
previous cervicofacial flap that involved the advanced portions of the flap and left oral commissure. The tumor extended onto the upper lip, oral commissure, and buccal mucosa. All affected areas were excised using rush permanent sections. The commissure was reconstructed with an intraoral rotation flap, the lower lip with simple undermining and advancement, and the cheek with a prefabricated supraclavicular flap. To date, there have been no recurrences or new atypical lesions.

CASE 4

The primary lesion on the left upper lip extended onto the left oral commissure, vermillion, and labial mucosa of the upper lip, and vermillion of the lower lip. A biopsy specimen showed LM. The lesion was removed with narrow margins, and the subsequent reconstruction used cheek advancement and lip rotation flaps. Within the next 6 years, several recurrent lesions were noted on the left upper lip and melolabial fold. For reconstruction, rotation flaps, a cervicofacial myocutaneous platysma flap, and a myocutaneous orbicularis flap were used. Two years later, a biopsy specimen of another recurrent lesion on the left cheek and upper lip revealed a 0.43-mm-thick LMM. This was excised with a 1-cm margin; a large cheek rotation flap was used for reconstruction. The biopsy specimen showed negative margins. Recently, another recurrent lesion on the left cheek and upper lip was excised twice with positive margins.

HISTOPATHOLOGIC FINDINGS

All biopsy specimens from LM lesions revealed similar histopathologic features. Microscopic examination from a recurrent lesion from case 4 revealed an atypical intraepidermal melanocytic proliferation over a scar (Figure 5). The pleomorphic melanocytes were arranged as single units and small nests along the dermoepidermal junction. In some areas, there was elongation of the rete ridges, whereas in others, there was epidermal atrophy. Solar elastosis was noted. The atypical cells showed hyperchromatic, enlarged, irregular nuclei and areas of pagetoid spread.

Biopsy specimens from the oral mucosal lesions of case 3 showed a proliferation of solitary, pleomorphic melanocytes with hyperchromatic nuclei along the basal and suprabasal layers (Figure 6). Biopsy specimens from one of the oral lesions of case 1 (shown in Figure 2) demonstrated confluent nests of atypical melanocytes within the lower portion of the epithelium (Figure 7). Focal pagetoid spread was noted. In another biopsy specimen from the buccal mucosa, a dermal spindle cell neoplasm was
Lentigo maligna occurs in white patients on sun-exposed areas, predominantly the head and neck. Extension onto mucosal surfaces such as the conjunctiva has been exceptional.28-30 Herein, we report 4 cases of LM with spread from perioral areas onto oral mucosa.

All patients had cutaneous lesions for several years before development of intraoral involvement. The lesions ran a chronic course complicated by several recurrences after surgery. Two of the patients never achieved complete remission, and all experienced significant long-term morbidity. Primary melanoma of the oral cavity can be excluded in our patients primarily by history. Metastatic melanoma from the skin to the oral cavity is extremely rare and can be ruled out by the absence of advanced primary skin tumor. Benign pigmented lesions such as melanocytic nevi, oral melanoacanthomas, and oral and labial melanotic macules can be excluded by the atypical histopathologic features.

The skin lesions showed typical histopathologic features of LM22-25 such as solitary and small nests of atypical melanocytes along the basal layer of the epidermis and adnexal structures, epidermal atrophy, and solar elastosis. Pagetoid spread, melanophages, and a dermal lymphohistiocytic infiltrate were sometimes seen. The histopathologic characteristics of the oral lesions were consistent with contiguous spread of the tumor from perioral skin areas.

Histopathologic evidence of invasion (LMM) was seen in 3 of the 4 patients at some point during their long course. While this is a small sample size, this suggests a higher than previously hypothesized progression of LM to LMM.24 The lesions may have progressed to an invasive stage because of prolonged radial growth phases secondary to incomplete cure after each recurrence. It has been shown that the risk for LMM increases proportionately with lesional diameter.25 Furthermore, LM may have progressed to LMM in areas that were not visible to the patient, thus being unnoticed for long periods of time. As seen in case 1, an invasive component was diagnosed in an oral LM of which the patient was not aware. Although development of invasive areas may occur slowly and gradually, there have been reports of rapid progression to LMM despite careful clinical follow-up.26,27 The recurrence of LM has been attributed to several factors, including migration of malignant melanocytes from adjacent epidermis or migration of deep adnexal melanocytes to the epidermal surface.1,2 Most authors believe that surgical excision is the treatment of choice, but the optimal surgical management of LM is still being defined. The recurrence rate with standard surgical excision (9%) is lower than that reported with destructive methods (35%-55%).28,29 The failure rate of standard excision may be due to microscopic extension of LM by as much as 1.5 to 3 cm beyond the clinical margins.30,31 In most cases presented herein, conventional surgery, even with wide margins, failed to eradicate the tumor completely and caused significant disfigurement.

The advocates of Mohs micrographic surgery for LM argue that this technique has a high cure rate, spares normal tissue, and allows examination of 100% of surgical margins.25 However, the value of frozen vs rush permanent sections is debatable.31-37 While some authors33 suggest that frozen sections are sensitive and specific for the diagnosis of melanoma, others32 argue that frozen sections contain artifacts and are often difficult to interpret. The use of rush permanent sections34,35 may eliminate these problems but carries the disadvantage that only 1 stage per day can be performed. A recent study32 recommended that if only frozen sections are to be performed, the final stage of surgery should be submitted for analysis of permanent sections prior to closing the wound. This ensures complete removal of the tumor while requiring only 2 to 3 mm of additional tissue. In this study, rush permanent sections were performed in cases 2 and 3 with excellent results.

In summary, we report 4 cases of cutaneous LM with extension onto oral mucosa. The significant morbidity associated with this clinical presentation is highlighted by the numerous recurrences and, in many instances, the need for major reconstruction with subsequent cosmetic disfigurement. This clinical presentation requires a high index of suspicion by the clinician. Examination of the oral mucosa should be performed in all patients with atypical pigmented perioral lesions. Furthermore, patients with peri-oral LM require long-term follow-up because there is a high probability of recurrence and/or progression to LMM.

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REFERENCES

3. Holman CDJ, Armstrong BK. Cutaneous malignant melanoma and indicators of


